

WHAT IS CLAIMED IS:

1. A bioreactor for producing functional cartilaginous tissue from a cell-seeded scaffold or a cell-seeded scaffold integrated with an osteoconductive and/or osteoinductive substrate, comprising:

5 (a) a growth chamber, and

(b) means for applying hydrostatic and/or deformational loading to the cell-seeded scaffold or cell-seeded scaffold integrated with an osteoconductive and/or osteoinductive substrate.

2. The bioreactor of Claim 1, wherein the scaffold is bioresorbable.

10 3. The bioreactor of Claim 1, wherein the scaffold is biocompatible.

4. The bioreactor of Claim 1, wherein the scaffold is biodegradable.

5. The bioreactor of Claim 1, wherein the scaffold is non-biodegradable.

6. The bioreactor of Claim 1, wherein means (b) applies intermittent cyclical hydrostatic fluid pressurization.

15 7. The bioreactor of Claim 6, wherein the fluid pressurization is from about 0 to about 18 MPa.

8. The bioreactor of Claim 7, wherein the fluid pressurization is from about 0 to about 6 MPa.

20 9. The bioreactor of Claim 6, wherein the cyclical frequency is from about 0 to about 5 Hz.

10. The bioreactor of Claim 9, wherein the cyclical frequency is from about 0.1 to about 2 Hz.

11. The bioreactor of Claim 1, wherein the fluid pressurization is applied for from about 0.5 to about 18 hours per day.

25 12. The bioreactor of Claim 11, wherein the fluid pressurization is applied for from about 2 to about 6 hours per day.

13. The bioreactor of Claim 1, wherein means (b) applies intermittent cyclical deformational loading.

14. The bioreactor of Claim 13, wherein the deformational loading is from about 0 to about 50%, based upon the thickness of the cell-seeded scaffold.

15. The bioreactor of Claim 14, wherein the deformational loading is from about 0 to about 20%.

5 16. The bioreactor of Claim 13, wherein the cyclical frequency is from about 0 to about 5 Hz.

17. The bioreactor of Claim 16, wherein the cyclical frequency is from about 0.1 to about 2 Hz.

18. The bioreactor of Claim 13, wherein the deformational loading is from
10 about 0.5 to about 18 hours per day.

19. The bioreactor of Claim 18, wherein the deformational loading is from about 2 to about 6 hours per day.

20. The bioreactor of Claim 1, wherein means (b) applies intermittent cyclical hydrostatic fluid pressurization and intermittent cyclical deformational loading.

15 21. The bioreactor of Claim 20, wherein the amplitude of the hydrostatic pressure and the amplitude of the deformational loading are modified over time as matrix elaboration proceeds.

22. The bioreactor of Claim 1, wherein the resulting tissue comprises hyaline cartilage.

20 23. The bioreactor of Claim 1, wherein the resulting tissue comprises hyaline cartilage and a osteoconductive and/or osteoinductive substrate.

24. The bioreactor of Claim 1, wherein the resulting tissue comprises elastic cartilage.

25 25. The bioreactor of Claim 1, wherein the resulting tissue comprises fibrocartilage.

26. The bioreactor of Claim 1 which comprises means for producing tissue in desired shapes.

27. The bioreactor of Claim 26, wherein the shaped tissue conforms to a body part, a prosthesis, a cosmetic implant, or a defect to be filled.

28. The bioreactor of Claim 1, wherein the loading platens which produce deformational loading conform to a body part, a prosthesis, a cosmetic implant, or a defect to be filled.

29. A method for producing functional cartilaginous tissue from a cell-seeded scaffold or a cell-seeded scaffold integrated with an osteoconductive and/or osteoinductive substrate, said method comprising the steps of:

(a) inoculating chondrocytes or chondroprogenitors into a scaffold or a scaffold integrated with an osteoconductive and/or osteoinductive substrate;

(b) placing cell-seeded scaffold or cell-seeded scaffold integrated with an osteoconductive and/or osteoinductive substrate into a bioreactor

(c) filling said bioreactor with liquid growth medium.

(d) applying hydrostatic pressurization and/or deformational loading to the cell-seeded scaffold or cell-seeded scaffold integrated with an osteoconductive and/or osteoinductive substrate; and

(e) culturing said stressed cell-seeded scaffold or cell-seeded scaffold integrated with an osteoinductive substrate for a time sufficient to produce functional cartilaginous tissue.

30. The method of Claim 29, wherein the bioreactor is the bioreactor of Claim 1.

31. The method of Claim 29, wherein the scaffold is biocompatible.

32. The method of Claim 29, wherein the scaffold is biodegradable.

33. The method of Claim 29, wherein the scaffold is non-biodegradable.

34. The method of Claim 29, wherein the scaffold is bioresorbable.

35. The method of Claim 29, wherein said stressed cells:

(a) display enhanced maintenance of a chondrocyte phenotype; and

(b) produce a functional cartilaginous matrix.

36. The method of Claim 29, wherein hydrostatic pressurization is applied by means comprising a reservoir, a pump, and tubing interconnecting said growth chamber, said reservoir, and said pump, so as to allow pressurization of liquid growth medium from said reservoir, in response to force applied by said pump.

37. The method of Claim 36, wherein said pump comprises a piston and chamber.
38. The method of Claim 29, wherein in step (d) intermittent cyclical hydrostatic fluid pressurization is applied.
- 5 39. The method of Claim 38, wherein the fluid pressurization is from about 0 to about 18 MPa.
40. The method of Claim 39, wherein the fluid pressurization is from about 0 to about 6 MPa.
41. The method of Claim 38, wherein the cyclical frequency is from about
10 0 to about 5 Hz.
42. The method of Claim 41, wherein the cyclical frequency is from about 0.1 to about 2 Hz.
43. The method of Claim 29, wherein the fluid pressurization is applied for from about about 0.5 to about 18 hours per day.
- 15 44. The method of Claim 43, wherein the fluid pressurization is applied for from about 2 to about 6 hours per day.
45. The method of Claim 29, wherein in step (d) intermittent cyclical deformational loading is applied.
46. The method of Claim 45, wherein the deformational loading is from
20 about 0 to about 50%, based upon the thickness of the cell-seeded scaffold.
47. The method of Claim 46, wherein the deformational loading is from about 0 to about 20%.
48. The method of Claim 45, wherein the cyclical frequency is from about 0 to about 5 Hz.
- 25 49. The method of Claim 48, wherein the cyclical frequency is from about 0.1 to about 2 hz.
50. The method of Claim 45, wherein the deformational loading is from about 0.5 to about 18 hours per day.
51. The method of Claim 50, wherein the deformational loading is from
30 about 2 to about 6 hours per day.

52. The method of Claim 29, wherein in step (d) intermittent cyclical hydrostatic fluid pressurization and intermittent cyclical deformational loading are applied.

53. The method of Claim 52, wherein the amplitude of the hydrostatic pressure and the amplitude of the deformational loading are modified over time as matrix elaboration proceeds.

54. The method of Claim 29, wherein the resulting tissue comprises hyaline cartilage.

55. The method of Claim 29, wherein the resulting tissue comprises hyaline cartilage and osteoinductive substrate.

56. The method of Claim 29, wherein the resulting tissue comprises elastic cartilage.

57. The method of Claim 29, wherein the resulting tissue comprises fibrocartilage.

58. The method of Claim 29 wherein the bioreactor comprises means for producing tissue in desired shapes.

59. The bioreactor of Claim 29 where the loading platens which produce deformational loading conform to a body part, a prosthesis, a cosmetic implant, or a defect to be filled.

60. The method of Claim 59, wherein the shaped tissue conforms to a body part, a prosthesis, a cosmetic implant, or a defect to be filled.